TRANSMITTAL LETTER (General - Patent Pending)	Docket No. PENN-0065

In Re Application Of: **Wolfe and Fraser**

Application No.	Filing Date	Examiner	Customer No.	Group Art Unit	Confirmation No.
08/393,066	February 23, 1995	Deborah Crouch	26259	1632	1030

Title: **METHOD OF DELIVERING GENES TO THE CENTRAL NERVOUS SYSTEM OF A MAMMAL**

COMMISSIONER FOR PATENTS:

Transmitted herewith is:

Supplemental Reply Brief

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Dated: **January 30, 2007**

Jane Massey Licata
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No.:	PENN-0065
Inventors:	Wolfe and Fraser
Serial No.:	08/393,066
Filing Date:	February 23, 1995
Examiner:	Deborah Crouch
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Electronically Submitted via EFS-Web
Date: **January 30, 2007**

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Commissioner for Patents
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SUPPLEMENTAL REPLY BRIEF

This is in response to the supplemental Examiner's Answer dated November 30, 2006, which raised certain issues that Appellants wish to address.

The Examiner alleges that Appellant has not provided any specification support for a use of the claimed method absent gene therapy. It is suggested that while precise predictability is not required, predictability without undue experimentation is the requirement for enablement. The Examiner suggests that the rejection has been made with support from Fink et al., Blomer et al. Eck et al. and Wolfe et al., whereas Appellant has not provided any evidence that at least 4 months of expression overcomes the concerns of these references. It is suggested that Fink et al. and Eck et al. outline the myriad problems associated with neurotrophic viral vectors such as HSV and set forth several factors which they state question the use of these vectors in gene therapy. The Examiner acknowledges that while expression for at least four months may be beneficial, there is no evidence the benefit is in gene therapy and can therefore provide a therapeutic effect.

Appellants respectfully disagree with the Examiner's reading of the cited references. The Examiner points to Fink et al., Blömer et al., Eck et al., and Wolfe et al. (*e.g.*, as cited in the Office Action mailed October 11, 2002) as an assessment of the state of the art of gene therapy at the time of the instant invention was made, citing problems of impracticality and unpredictability such as the levels and duration of gene expression for effective treatment, residual toxicity resulting from non-replicating vectors and silencing DNA sequence expression from persisting latent HSV genomes in neurons, and spread and cytotoxicity of HSV.

It is respectfully submitted that such selective reading of these references, in which statements regarding the state of gene therapy at the time of filing of the present invention are taken out of context, has resulted in a mischaracterization of the

references that cannot validly be relied on to support an allegation of unpredictability of gene therapy. For example, the abstract of Eck et al. mentions how gene therapy has overcome barriers of the former cellular inaccessibility of large proteins encoded by therapeutic genes. The article provides several examples of the progress made in developing delivery systems for gene therapy, its applications not only in inherited single-gene defects, but also in acquired illnesses such as cancer, cardiovascular and infectious diseases, and continual advancement for strategies to introduce recombinant DNA into tissues in a selective manner.

Although Eck et al. acknowledge that gene transfer was not an established clinical treatment regime, it clearly had been demonstrated, based on actual clinical trial data, that therapeutically relevant genes could be transferred into human patients and be expressed within the patient in such a manner as to show biologic efficacy. Eck et al. further provide a summary of the studies demonstrating that transfer of genes to humans is feasible (see Table 5-1, pp. 80-81) and statistics concerning the numbers and outcomes of human gene transfer studies. Eck et al. conclude that human gene therapy, although still in its infancy, offers the possibility for "major advancements in the prevention and treatment of myriad diseases." They also conclude that "as increasing numbers of investigators address these issues, better reagents likely will emerge." See column 2 at page 99.

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. Thus, the test of enablement is not

whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

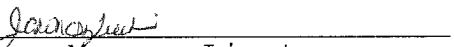
In this regard, Appellants are not aware of any requirement under current U.S. patent law specifying particular minimum levels of optimization and certified efficacy in order for a treatment-related area of art to qualify as sufficiently "predictable" under 35 U.S.C. §112, first paragraph. The relevant standard is not that of an established, fully optimized, clinical course of treatment; rather, even in an unpredictable art, a patent application satisfies the requirements of 35 U.S.C. §112, first paragraph, so long as it provides sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the claimed subject matter with reasonable, but not undue, experimentation. There is no requirement that a method achieve a specified level of efficacy or efficiency in order to be considered "enabled" by the specification. As such, it is respectfully submitted that although the art of gene therapy may not have been in routine clinical practice at the effective filing date of the subject application, it was not so unpredictable as to qualify as a major factor in the determination of whether the requirements of 35 U.S.C. §112, first paragraph, are satisfied with respect to the instantly claimed subject matter.

In any event, the grounds for rejection of the present claims under 35 U.S.C. §112, first paragraph, are primarily based on the alleged unpredictability of the art of gene therapy in general. The issue of whether the instant claims are enabled by the specification should not turn on the state of the art of gene therapy as has been maintained by the Examiner during the prosecution of this application. Instead, the relevant question with regard to the enablement of the subject matter of the instant claims is whether the particular steps and materials of the claimed

method are described in the specification in such a way as to enable one skilled in the art to make and use the subject matter *as claimed*.

Appellants are claiming subject matter that has been reduced to practice, as specified in MPEP 2164.02. Using the knowledge in the art and the teachings in the application, the full breadth of the claims are clearly enabled, such that they can be practiced without undue experimentation. Thus, contrary to the Examiner's conclusion, undue experimentation is not required on the part of the skilled artisan in order to carry out the present invention and, therefore, the enablement requirement under 35 U.S.C. 112, first paragraph, has been met.

Respectfully submitted,



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DATE: January 30, 2007

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